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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/645,546	08/22/2003	Bruce K. Krueger	028754-042	9617

21839 7590 09/09/2005

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EXAMINER	
MONTANARI, DAVID A	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 09/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/645,546	KRUEGER ET AL.	
	Examiner	Art Unit	
	David Montanari	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,13-16 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,13-16 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: _____.

S.D

DETAILED ACTION

1. Applicants arguments and amendments filed on June 9th, 2005 have been entered.

2. Claims 1, and 13-14 have been amended.

3. Claims 4-12, 17, and 19-54 have been cancelled.

4. Rejection of claims 1-3, 13-16, and 18 under 35 U.S.C. 102(b) has been withdrawn.

5. Rejection of claims 1-3, 13-16, and 18 under 35 U.S.C. 112, second paragraph has been withdrawn.

6. Rejection of claims 1-3, 13-16, and 18 under 35 U.S.C. 112, first paragraph-written description has been withdrawn.

7. Claims 1-3, 13-16, and 18 are examined in the instant application.

Claim Objections

Claims 1, and 13 are objected to because of the following informalities: Claims 1 and 13, after amendment to said claims have the following recitation "contacting a neuropathic hippocampal neurons". However, "neurons" should be changed to "neuron" so that proper agreement exits. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 13-16, and 18 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of contacting a neuropathic hippocampal neuron under *in vitro* conditions with an amount of isolated nucleic acid encoding full-length TrkB whereby said amount of said isolated nucleic acid is sufficient to increase the amount of full-length TrkB in said neuron compared to an untreated neuron, does not reasonably provide enablement for a method of contacting a neuropathic hippocampal neuron under *in vivo* conditions with an amount of isolated nucleic acid encoding full-length TrkB whereby said amount of said isolated nucleic acid is sufficient to increase the amount of full-length TrkB in said neuron compared to an untreated neuron. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims for reasons of record in the office action dated 3/10/2005.

Claims 1-3, 13-16, and 18 are drawn to methods of treating a neuro-degenerative disorder or a neuro-developmental disorder comprising contacting a neuropathic hippocampal neuron with an amount of an isolated nucleic acid encoding full-length TrkB where the result is an increase in the amount of TrkB in a treated hippocampal neuron over a non-treated hippocampal neuron.

Applicants arguments in amendment filed June 9th, 2005 have been fully considered but are not persuasive.

Applicants argue in amendment that the disclosure of an *in vitro* use for TrkB, combined with the examiner's admission that the present claims enable the use of TrkB *in vitro*, is sufficient to enable the amended claims for *in vivo* use because a rigorous or an invariable exact

correlation between *in vitro* and *in vivo* is not required as stated in *Cross v. lizuka* or *In re Brana.* Applicants continue to argue that the specification discloses a well-known animal model of a neurodegenerative disease, the Ts16 mouse model of Down's Syndrome, which provides sufficient enablement for the scope of applicant's claimed invention. Applicants continue to argue that MPEP § 2164.02 states "If the art is such that a particular model is recognized as correlating to a specific condition, than it should be accepted as a correlating unless the examiner has evidence that the model does not correlate". However, these arguments are not persuasive. MPEP § 2164.02 states with reference to *Cross vs lizuka* :

> Since the initial burden is on the examiner to give reasons for the lack of enablement, the examiner must also give reasons for a conclusion of lack of correlation for an *in vitro* or *in vivo* animal model example. A rigorous or an invariable exact correlation is not required, as stated in *Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 USPQ 739, 747 (Fed. Cir. 1985):

The examiner has presented reasons of record why there is lack of correlation for an *in vitro* treatment of hippocampal neurons that cannot be extrapolated to an *in vivo* treatment of hippocampal neurons. In the previous office action, the examiner states that the art teaches the significant unpredictability of gene therapy and neurodegenerative disorders. Further the examiner stated that hippocampal neurons are taught in the art to be particularly difficult to target by viral vectors *in vivo* (OA, 3/10/2005, pg. 6 lines 5-9). The examiner has stated several lines of evidence covering a variety of gene delivery systems are each unpredictable for the treatment of a neurodegenerative disorder *in vivo*, including adenoviruses, liposomes, the herpes virus, and naked DNA. Applicants arguments concerning the animal model of the Ts16 mouse (Downs Syndrome) to evaluate the *in vivo* treatment of a neuron with an isolated nucleic acid encoding full-length TrkB are also unpersuasive by the fact that Ts16 transgenic mice are

embryonic lethal (Bambrick et al. 1995, PNAS, Vol. 92, pg. 9692, col. 2 parag. 1 lines 15-16). The skilled artisan would find significant unpredictability in working with a disease animal model for developing a therapeutic treatment if the test animal does not survive to birth (i.e. cognitive recognition test, memory tests, and behavior pattern tests are difficult to do with dead animals). When the Ts16 mouse model is considered to be enabling in view of *In re Brana*, there is sufficient evidence to support the fact that using the Ts16 animal model for *in vivo* treatment of a neurodegenerative disease is not enabled when examined in view of the scope of the claimed invention. Applicants have only demonstrated that TrkB levels in isolated Ts16 hippocampal neurons can be increased by treatment with a nucleic acid encoding full-length TrkB, no treatment of any disease is disclosed by the specification. Further there is no disclosure in the specification linking TrkB levels with Down's Syndrome or any other neurodegenerative disease. Thus for reasons of record and above the rejection is maintained.

No claims are allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Montanari whose telephone number is 1-571-272-3108. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 1-571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

RAM R. SHUKLA, PH.D.
SUPERVISORY PATENT EXAMINER